

## **Supplementary Figures**

Isoeugenol is a selective potentiator of camptothecin cytotoxicity in vertebrate cells lacking TDP1

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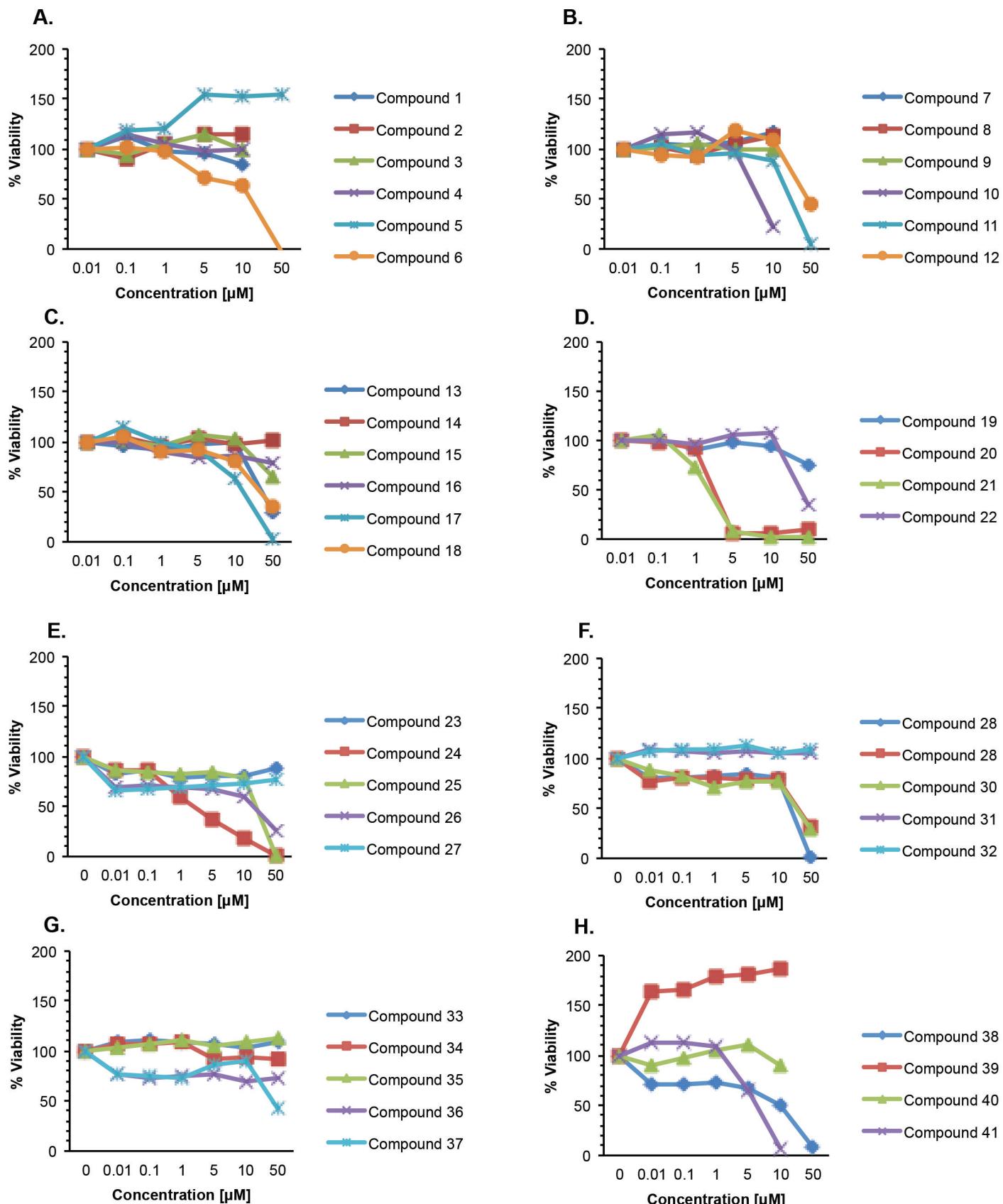
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# Joint first authors

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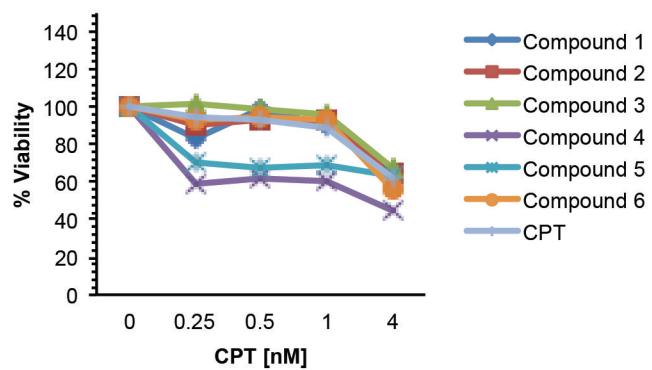
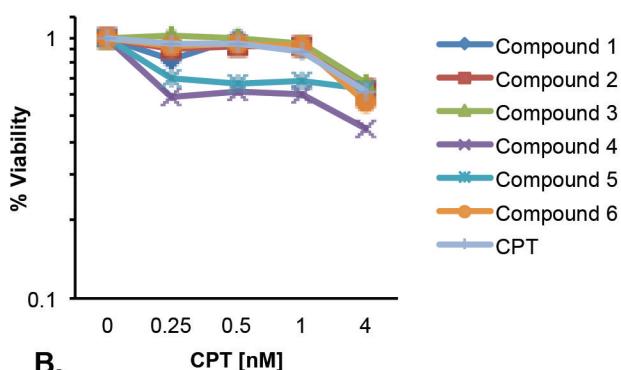
## Supplementary figure 1



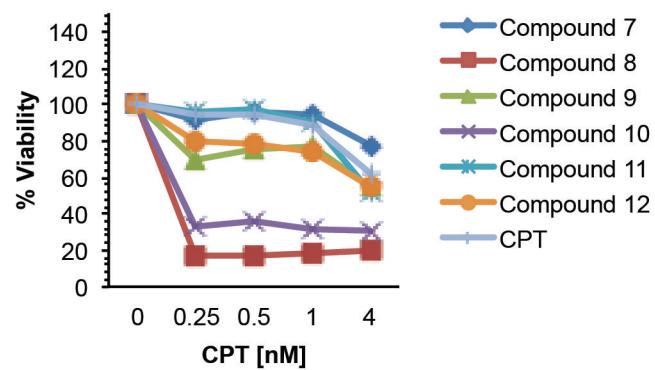
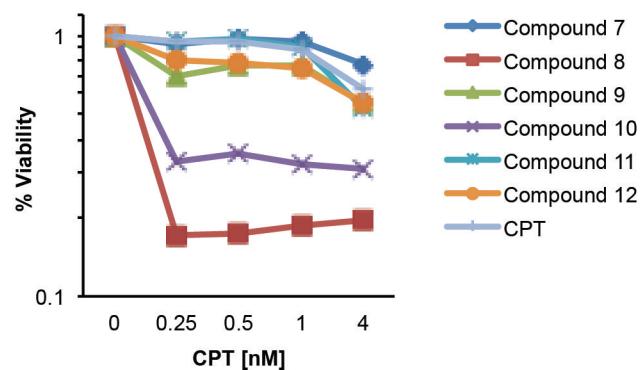
**Supplementary figure 1. The cytotoxic effect of library compounds against Tdp1<sup>-/-</sup> DT40 cells . (A-H) Viability graphs indicating the cytotoxicity of compounds 1 to 41 at six different concentrations (0.01, 0.1, 1, 5, 10, and 50  $\mu$ M).**

## Supplementary Figure 2

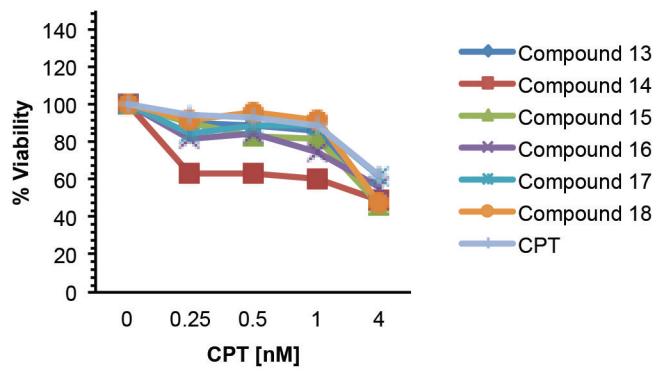
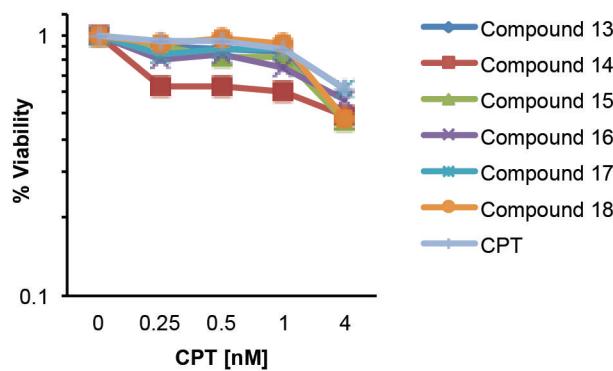
**A.**



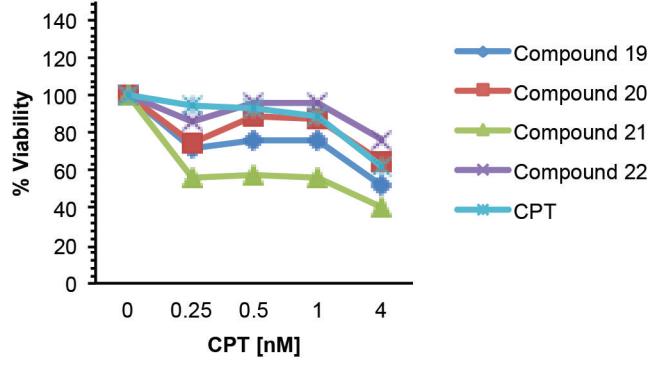
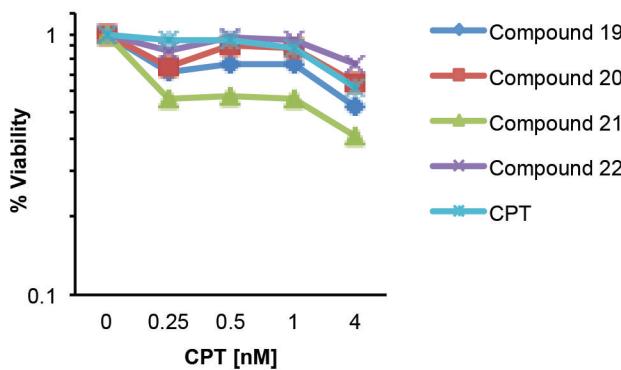
**B.**



**C.**

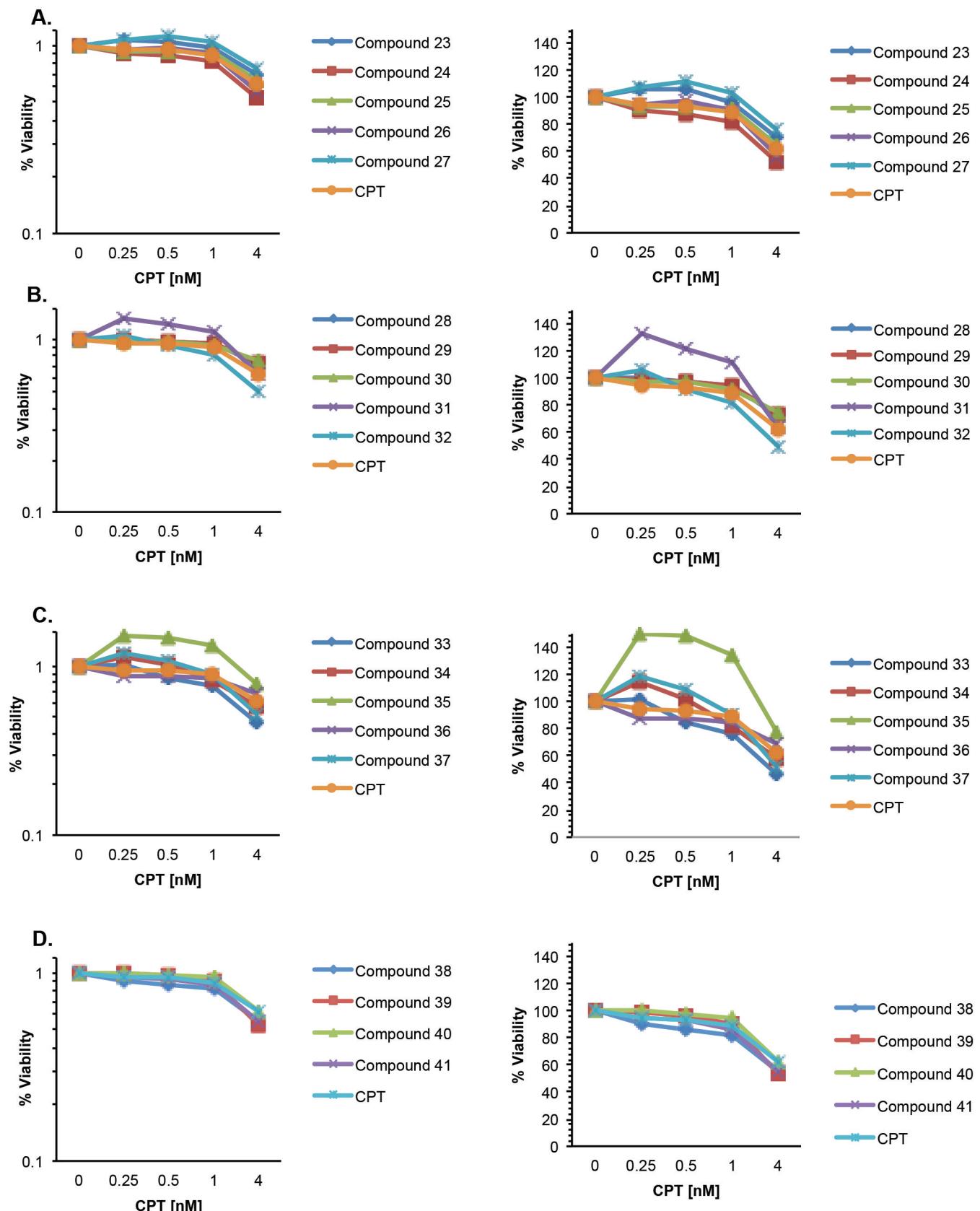


**D.**



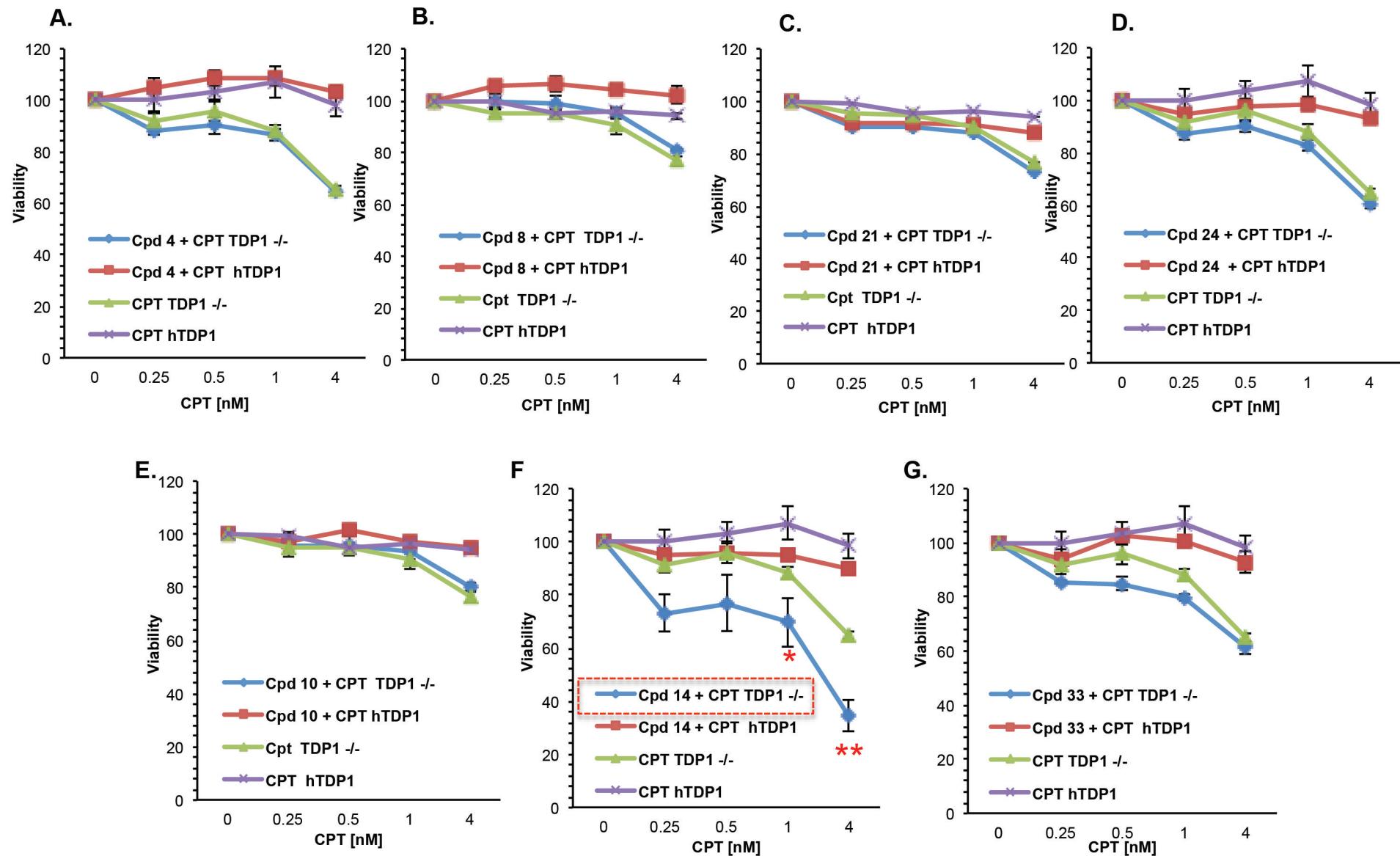
**Supplementary Figure 2. (A-D)** Primary screen of DT40 TDP1<sup>-/-</sup> cells against sublethal concentrations of compounds 1 to 22 in combination with CPT at four concentrations (sublethal: 0.25, 0.5, and 1 nM; lethal: 4 nM). **Left:** semi log graph; **right:** percentage representation.

### Supplementary Figure 3



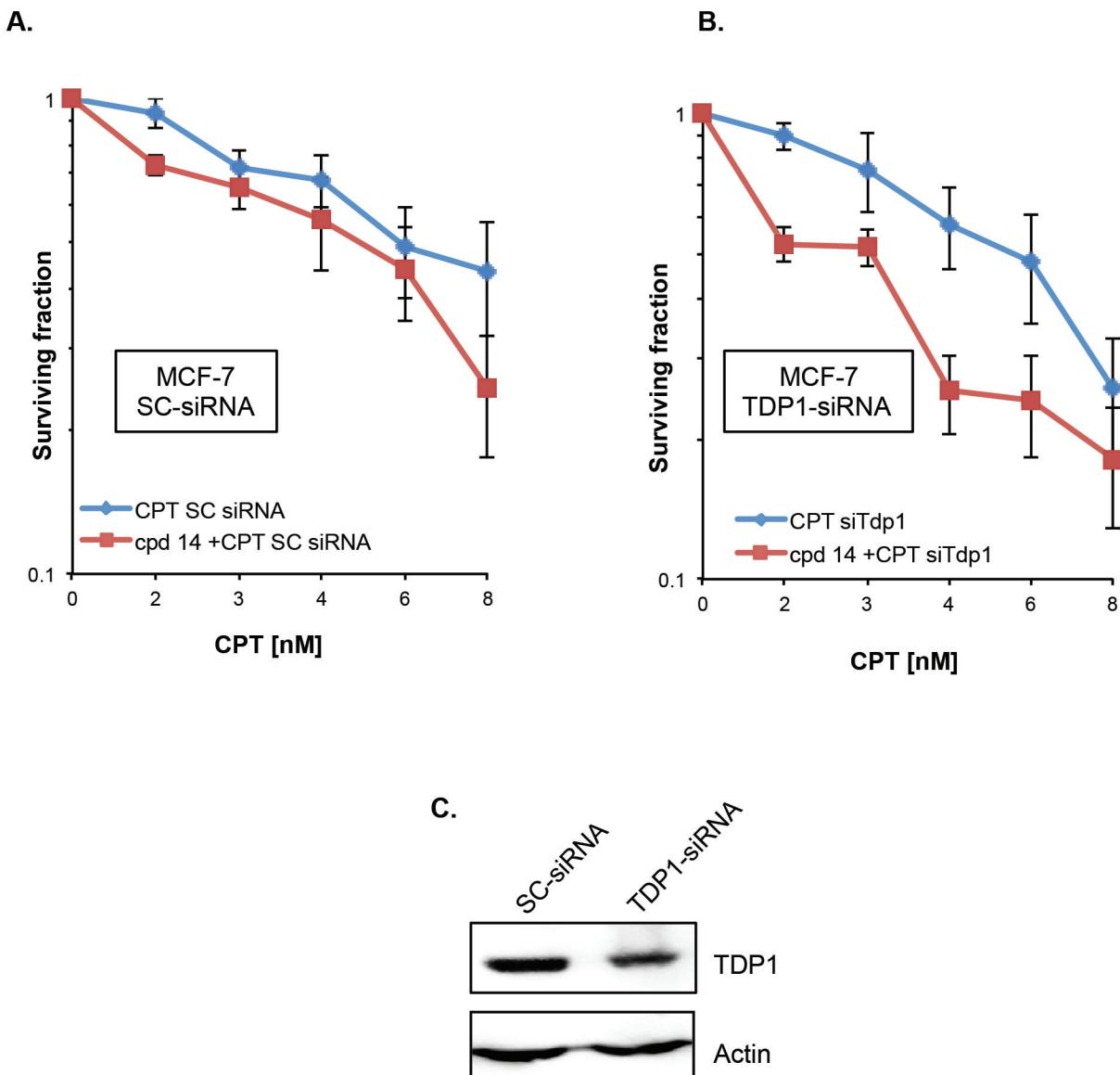
**Supplementary Figure 3.** (A-D) Primary screen of DT40 Tdp1<sup>-/-</sup> cells against sublethal concentrations of compounds 23 to 41 in combination with CPT at four concentrations (sublethal: 0.25, 0.5, and 1 nM; lethal: 4 nM). Left: semi log graph; right: percentage representation.

## Supplementary Figure 4



**Supplementary Figure 4. Isoeugenol potentiates the cytotoxic effect of CPT in a TDP1-dependent manner.** Same data as shown in Figure 1 but the viability is presented as % instead of semi-log scale

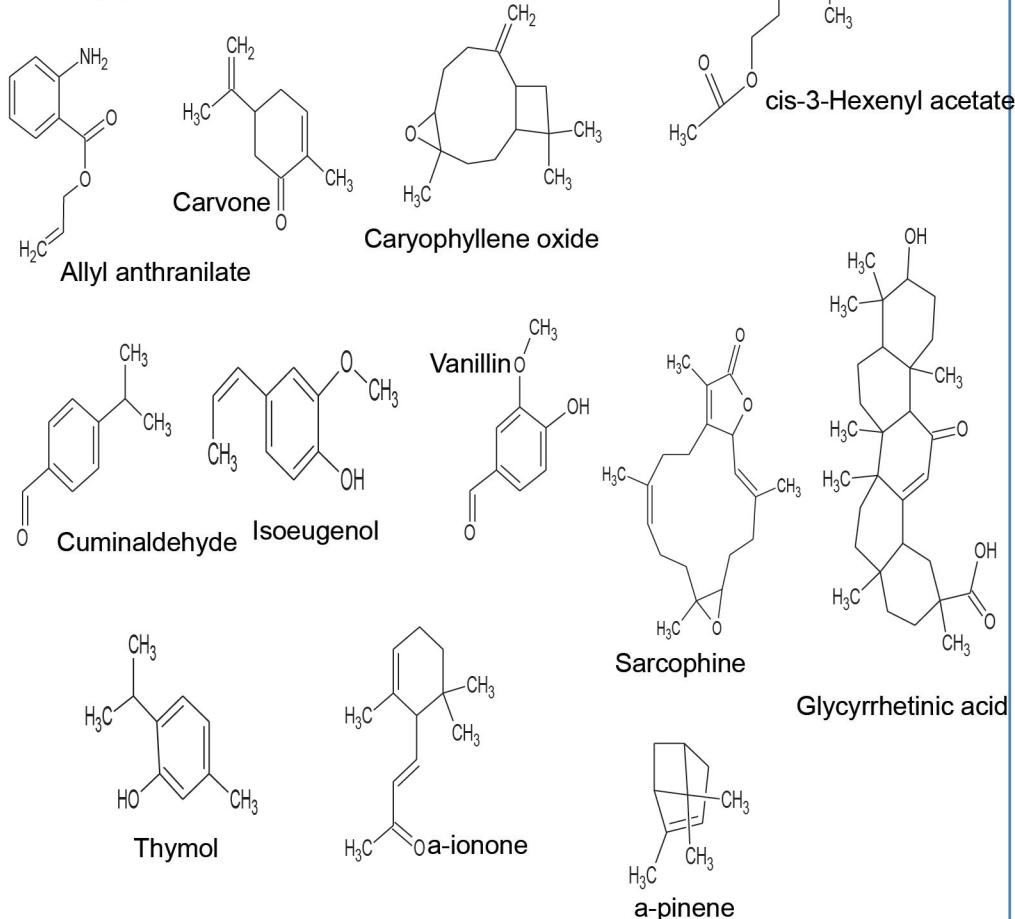
## Supplementary figure 5



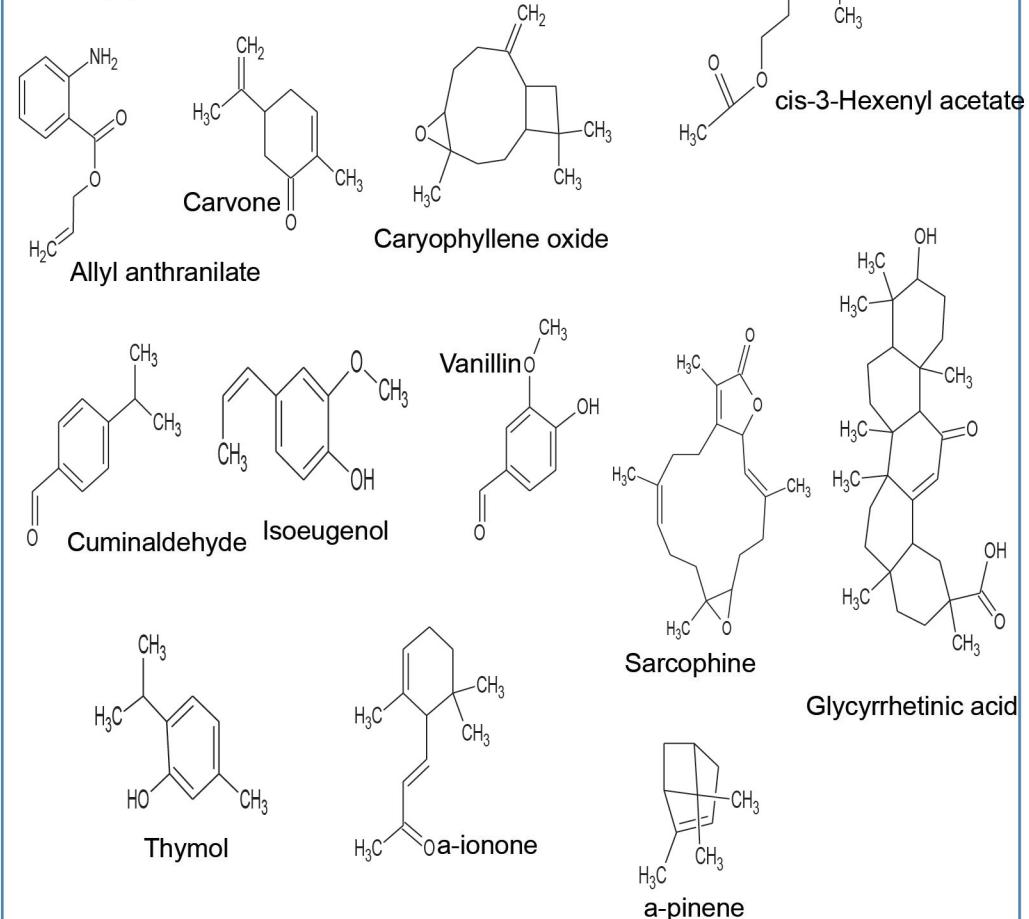
**Supplementary figure 5. Isoeugenol potentiates CPT cytotoxicity in TDP1 depleted human cells.** MCF-7 cells were treated with a scrambled siRNA “SC-siRNA” (A) or TDP1 siRNA “TDP1-siRNA” (B) and survival was examined using clonogenic survival assays at the indicated doses of CPT (1 lethal and four sub-lethal: 8nM, 6nM, 4nM, 3nM and 2nM; resp.) in presence or absence of a sub-lethal concentration of compounds 14 (4  $\mu$ M). Survival was calculated by dividing the average number of colonies on treated plates by the average number of colonies on untreated plates. Data are the average  $\pm$  s.e.m. of three biological replicates. (C) Cell lysates from A and B were fractioned by SDS-PAGE and analysed by immunoblotting.

## Supplementary figure 6

### Terpenoids/ Phenylproanoids



### Terpenoids/ Phenylproanoids



**Supplementary Figure 6.** Structures of flavonoids, phenolic acids, and Terpenoids/ Phenylproanoids.

### Phenolic acids

